

Annotation: Neurofeedback – train your brain to train behaviour

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Background: Neurofeedback (NF) is a form of behavioural training aimed at developing skills for self-regulation of brain activity. Within the past decade, several NF studies have been published that tend to overcome the methodological shortcomings of earlier studies. This annotation describes the methodical basis of NF and reviews the evidence base for its clinical efficacy and effectiveness in neuropsychiatric disorders. **Methods:** In NF training, self-regulation of specific aspects of electrical brain activity is acquired by means of immediate feedback and positive reinforcement. In frequency training, activity in different EEG frequency bands has to be decreased or increased. Training of slow cortical potentials (SCPs) addresses the regulation of cortical excitability. **Results:** NF studies revealed paradigm-specific effects on, e.g., attention and memory processes and performance improvements in real-life conditions, in healthy subjects as well as in patients. In several studies it was shown that children with attention-deficit hyperactivity disorder (ADHD) improved behavioural and cognitive variables after frequency (e.g., theta/beta) training or SCP training. Neurophysiological effects could also be measured. However, specific and unspecific training effects could not be disentangled in these studies. For drug-resistant patients with epilepsy, significant and long-lasting decreases of seizure frequency and intensity through SCP training were documented in a series of studies. For other child psychiatric disorders (e.g., tic disorders, anxiety, and autism) only preliminary investigations are available. **Conclusions:** There is growing evidence for NF as a valuable treatment module in neuropsychiatric disorders. Further, controlled studies are necessary to establish clinical efficacy and effectiveness and to learn more about the mechanisms underlying successful training. **Keywords:** Neurofeedback, electroencephalogram (EEG), frequency bands, slow cortical potentials (SCPs), attention-deficit hyperactivity disorder (ADHD), epilepsy, self-regulation.

Mental states are reflected in the electroencephalogram (EEG), the recording of brain electrical activity via electrodes placed on the human scalp. A relaxed state (with eyes closed) is characterised by rhythmic oscillations in the alpha (8–13 Hz) band. In contrast, an attentive/aroused state is reflected by predominant higher-frequency, low-amplitude activity (beta, 13–30 Hz). Such a beta activity pattern characterises, e.g., the EEG of a musician during a concert or the EEG of a child during an anxiety state ('tonic activation'). In the context of particular events, other patterns (components) can also be seen in the EEG besides the spontaneous oscillations. If the musician has to play a solo, his attention and preparation effort increase steadily during the bars preceding the solo in order to play the first note precisely. In the recording, an increasing slow negative shift (slow cortical potential, SCP; see Table 1) develops, reflecting the phasic attentional and preparatory activation (Rockstroh, Elbert, Birbaumer, & Lutzenberger, 1982).

Furthermore, the spontaneous EEG and event-related potentials (ERPs) allow tracking of developmental effects (Rothenberger, Banaschewski, Siniatchkin, & Heinrich, 2003) and EEG and ERP

studies revealed important findings concerning the pathophysiological background of child psychiatric disorders and the mechanism of therapeutic interventions (Banaschewski & Brandeis, in press). Thus, recording of brain electrical activity is one of the most important methods to investigate the brain-behaviour relationship in children and adolescents.

The question as to what extent the modulation of brain electrical activity patterns can be learned and whether changes (improvements) at the behavioural level may be achieved by this process leads to the concept of neurofeedback (NF). NF activities in the field of child and adolescent psychiatry started about 30 years ago (Lubar & Shouse, 1976). Treatment outcome has been most intensively studied in ADHD and epilepsy. However, NF has been ignored by the scientific community and at best been criticised, since controlled research was lacking. In the meantime, more and better data have become available and NF has become more popular.

In this annotation, the methodical basis of NF and training paradigms will be described.

The evidence base for the clinical efficacy and effectiveness of NF in neuropsychiatric disorders, with a focus on ADHD and epilepsy, will be reviewed. Finally, future directions of NF in clinics and research will be outlined.

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Box 1 EEG frequency bands and slow cortical potentials (SCPs)

The electroencephalogram (EEG) represents the spontaneous, ongoing electrical activity of the brain (mainly the cortex). Cortical activity is regulated by subcortical structures (particularly the thalamus). Traditionally, the EEG is divided into different frequency bands, e.g. delta (<4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz). The sensorimotor rhythm (SMR, 12–15 Hz) recorded over sensorimotor areas may be associated with thalamo-cortical inhibition. The spectral content of the EEG reflects, e.g., mental states and brain development (Niedermeyer & Lopes Da Silva, 2004).

Slow cortical potentials (SCPs), lasting from several hundred milliseconds to several seconds, are related to the level of excitability of underlying cortical regions. They originate in the apical dendritic layers of the neocortex. Surface-negative SCPs reflect synchronised depolarisation of large groups of neuronal assemblies (= increased excitation). They are recorded during states of behavioural or cognitive preparation and during motivational states of apprehension and fear. Surface-positive SCPs are thought to indicate reduction of cortical excitation of the underlying neural networks and appear during behavioural inhibition and motivational inertia. In cognitive tasks, the amplitude of a slow negative shift is thought to be related to the construct of resource allocation, i.e., the larger the amplitude the more resources of a particular type are allocated to a task. Fronto-striatal networks play an important role in SCP generation (Birbaumer, Elbert, Canavan, & Rockstroh, 1990; Hinterberger et al., 2003; Rösler, Heil, & Röder, 1997).

Methodical basis of NF and training paradigms

Biofeedback is an operant conditioning procedure in which participants (patients) learn to gain self-control over physiological functions (e.g., muscle activity, respiration, heart rate) that usually are not consciously perceived or controlled (Schwartz & Andrasik, 2003). Measures representing these functions are converted into visual or acoustic signals which are continuously fed back in real time. Changes that are made in the desired direction are rewarded, i.e., positively reinforced. Biofeedback training can be run as a kind of computer game and is thus principally attractive for children. The type of biofeedback using a measure derived from electrical brain activity is called neurofeedback (EEG biofeedback).

A complete NF training usually comprises 25–50 sessions of 45–60 minutes' duration. In the beginning a blocked training may be preferable to facilitate the neuromodulatory learning process.¹ To ensure transfer of the skill into everyday life, transfer trials, i.e., trials without contingent feedback, can be interspersed throughout the training. Furthermore, children should be instructed to practise their strategies at home and real-life situations should be integrated into the treatment.

Frequency training

In frequency training, either activity (maximum amplitude, energy) in one or several EEG frequency bands or the ratio of activity in different frequency bands has to be increased or decreased at a certain electrode position. In a paradigm often applied in ADHD, the goal is to decrease activity in the theta band and to increase activity in the beta band (or to decrease theta/beta ratio) at the vertex (electrode Cz). This may be achieved by an attentive but relaxed state (Lubar, 2003; see also Table 1).

Frequency training may be realised as follows: The activity of each frequency band to be trained is represented by a bar (varying in size) on a screen.

¹ Empirical data concerning an 'optimal' training setting do not exist.

Additionally, if activity in every frequency band is modulated in the desired way, a figure moves on the screen and points are gained (like in a computer game) or a reinforcing video sequence proceeds.

Usually, at the beginning of a session, baseline (average) values are determined during a 2–3 minute resting condition followed by several trials of, e.g., 5 minutes in length. Training sessions include about 20–40 minutes of neuroregulation exercises. Reward thresholds are adjusted so that the reward is received about 60–70% of the time. Using a moving time window of about 1–2 seconds in lengths, feedback is calculated several times per second so that the participant gets the impression of an online procedure.

SCP training

Healthy subjects can learn to modulate their SCPs in a biofeedback condition. Self-control is usually achieved within one to five training sessions (Elbert, Rockstroh, Lutzenberger, & Birbaumer, 1984). In most studies, negative SCPs (increased excitation) and positive SCPs (decreased excitation) had to be generated over the sensorimotor cortex (feedback electrode Cz). Rockstroh, Elbert, Lutzenberger, and Birbaumer (1990) reported that children are also able to learn SCP regulation.

A feedback and some technical information scene from an SCP training session are illustrated in Figure 1. The task is to change the colour of an object on the screen from white to red in negativity trials and from white to blue in positivity trials; i.e., the colour of the object (colour spectrum blue–white–red) represents the current SCP amplitude value. In other feedback animations, the SCP amplitude is represented by the vertical position of an object (e.g., aeroplane) flying from the left side to the right side of the screen during a trial.

An SCP trial typically consists of a 2 sec baseline period and a 6 sec feedback phase. Within a training session there may be, e.g., 120 trials divided into two or three blocks of 40–60 trials. Usually transfer trials (i.e., trials without contingent feedback) are trained in one of these blocks.

Table 1 Neurofeedback paradigms

Neurofeedback paradigm	Feedback electrode	Hypothesized training effects	Neuropsychiatric disorders
Frequency training Decrease of theta activity and increase of beta (e.g. 13–20 Hz) activity	Cz, C3	increase of arousal	ADHD (combined type, inattentive type)
Increase of SMR activity plus decrease of theta activity	central leads Cz, C4	increase of thalamo-cortical inhibition	epilepsy tic disorders ADHD (combined type, hyperactive/impulsive type)
Increase of theta/alpha ratio	Pz	increase of energy, well-being and empowerment	anxiety
Training of slow cortical potentials (SCPs) Generation of negative and positive SCP	Cz	improved regulation of cortical excitability	epilepsy (focus on decreasing excitability) ADHD

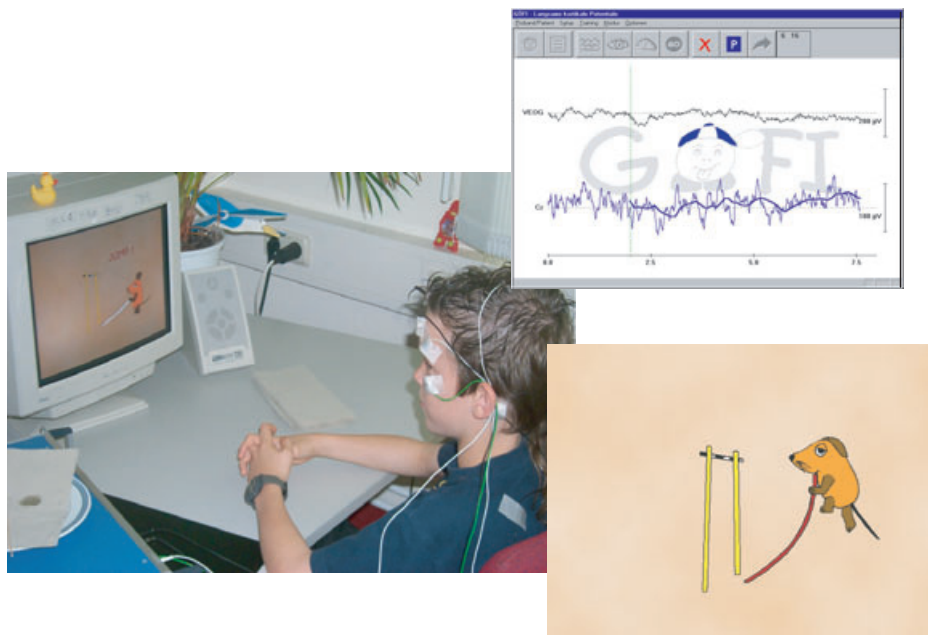


Figure 1 A boy sits in front of a computer monitor and plays a kind of computer game by modulating his brain electrical activity. The example presented is from an SCP training. The Mouse, a character from a popular German TV programme, wants to make a pole-vault. In negativity (positivity) trials the colour of the pole has to be changed from white to red (blue) so that the Mouse can jump at the end of a trial. The trial consists of a 2 sec baseline phase and a 6 sec feedback phase. At the end of the baseline phase (marked by the green line on the therapist’s monitor, a baseline (reference) value is determined by calculating the mean amplitude for this period. During the feedback phase, the mean SCP amplitude (moving time window, e.g., 1 sec) is calculated ten times per second and the colour of the pole (colour spectrum blue–white–red) changes according to the SCP amplitude related to the baseline value. Hence, the child has the subjective impression of an online procedure. Before each calculation, the EEG is controlled for artefacts by the NF software. The therapist can inspect the recorded signals (EEG channel: Cz; vertical electrooculogram, VEOG) on a separate monitor (‘dual-monitor solution’). The mouse was used with kind permission from WWF Lizenzhans Kålm

Artefacts

The EEG is easily contaminated by eye and head movements as well as muscle activity. These kinds of artefacts must be controlled and, if possible, corrected online by the NF software (Kotchoubey, Schleichert, Lutzenberger, & Birbaumer, 1997). An NF system with a separate monitor for the therapist showing the recorded signals is recommended (‘dual-monitor solution’).

Children must be aware of how to avoid artefacts. Otherwise, neuroregulation cannot be learned reli-

ably. This holds particularly true for SCP training in which more sensitive amplifiers are used.² Some technical effort as well as close monitoring of a child’s behaviour may be necessary to gain satisfactory signal quality.

² In SCP training, amplifiers with a high-pass frequency of 0.01 Hz or lower are used. Swallowing, tongue movements or breathing can produce artefacts of several hundred microvolts in this low frequency range.

NF trainer

NF training should be attended by a psychologically (skills in cognitive-behaviour therapy) and neuro-physiologically (basic knowledge about the EEG, including technical issues) educated person who is also familiar with the disorder of the participant.

The trainer has to select an adequate training protocol and to convey the concept of the NF training to the participant. Particularly in children, a main focus lies on assisting them to acquire adequate regulation strategies and keeping up their motivation. With respect to signal quality, a proper montage of the electrodes is required and the trainer should instruct the participant in how to minimise artefact-producing behaviour. Further important tasks of the trainer are to prepare and discuss 'homework' (practice of the strategies at home) and to support the participant in detecting critical daily-life situations which are appropriate to implement the learned regulation skills.

Evidence base for NF

NF in non-clinical subjects

Frequency training. Gruzelier and colleagues compared different paradigms of frequency training and control conditions in a series of studies with healthy adults (Egner & Gruzelier, 2001, 2003, 2004; Egner, Zech, & Gruzelier, 2004; Vernon et al., 2003). Pre-post comparisons of performance in cognitive tasks combined with EEG and ERP recordings, as well as in real life-situations, were reported:

- Egner and Gruzelier (2004) allocated 25 music students randomly to one of three training groups: sensorimotor rhythm (SMR, 12–15 Hz) training ($N = 9$), low-beta (15–18 Hz) training ($N = 8$), or a control condition ($N = 8$). NF training comprised 10 once-weekly training sessions of 15 minutes' duration. Subjects of the SMR group had to increase SMR activity and decrease theta (4–8 Hz) and 'high beta' (22–30) activity. The low-beta paradigm was to increase 15–18 Hz activity without concurrent rises in theta and 'high beta' activity. The Alexander technique was used as a control condition because it is the most widely practised behavioural training in professional orchestral musicians. Before and after training, subjects performed a continuous performance test (Test of Variables of Attention, TOVA³; Greenberg, 1987) and ERPs

³ The TOVA is a visual continuous performance test in which two easily discriminated visual stimuli are presented for 100 ms every 2 seconds. Subjects are instructed to respond to the target stimulus which is presented in 22.5% of the trials during the first half of the test and in 77.5% of the trials during the second half. The test lasts for 22.5 min. Scores (scales) derived from the test are omission errors, commission errors, mean reaction time and variability. There seem to be no test-retest practice effects.

were recorded in a selective attention task.

Whereas there were no pre-post effects in the control group, the low-beta group and the SMR group showed differential patterns. SMR training was associated with increased perceptual sensitivity in both tasks, as well as reduced omission errors and reaction time variability in the selective attention task. These effects of SMR training were explained by improved regulatory control in the sensorimotor pathway leading to more efficient higher-order attention processing. The low-beta group exhibited faster reaction times and increased target P300 amplitudes after training, probably reflecting higher general cortical background activation when processing the test.

- Vernon et al. (2003) reported that healthy adults could learn to increase their SMR activity while simultaneously inhibiting theta and beta (18–22 Hz) activity. After this type of NF training, subjects showed improvement in a semantic working memory task.
- Egner and Gruzelier (2003) assessed the impact of alpha/theta training (increase of theta/alpha ratio) on musical performance in students. The performance on stage improved only after alpha/theta training but not after other NF training paradigms or a control training according to ratings by blinded experts.
- The effects of NF training on the spectral topography of the EEG were studied in Egner et al. (2004). Subjects were randomly allocated to either SMR, beta, or alpha/theta training (feedback electrode: Cz). SMR training was found to be associated to a smaller extent with reduced post-training low-beta activity in the resting EEG, while, more reliably, alpha/theta training was associated with reduced relative frontal beta band activity. These results indicate that NF training of frequency components may affect spectral EEG topography in healthy subjects, but that these effects do not necessarily correspond to either the frequencies or the scalp locations addressed by the training paradigms.

Though sample sizes were small, these studies have shown specific effects for particular NF paradigms on attentional and working memory processes. In other words, different paradigms led to different effects at the cognitive as well as at the neurophysiological level. These results argue against the objective that training effects are merely caused by the fact that the training is an attention-demanding task. They also indicate that 'normal' subjects, i.e., persons without neuropsychiatric disorders, may profit from NF training ('peak performance').

SCP training. Since the 1980s it has been known that SCP changes learned in NF training are correlated with changes at the behavioural (performance) level and that the effects are not exclusively related

to non-specific phasic alertness (for review see Elbert, Rockstroh, Lutzenberger, & Birbaumer, 1984). It was demonstrated that mathematical tasks were solved more rapidly when subjects produced negativities. Furthermore, it was shown that it is also possible to learn left- and right-hemispheric SCP differences over the sensorimotor cortex (electrodes C3 and C4), resulting in decreased reaction times in tactile discrimination tasks for the hand contralateral to a self-generated negativity.

Hinterberger et al. (2003) examined the relationship between negative and positive SCPs and changes in the fMRI BOLD signal of adults who were trained to successfully self-regulate SCPs at Cz. fMRI revealed that the generation of negativity was accompanied by widespread activation in central, dorsolateral prefrontal, and parietal brain regions as well as in the basal ganglia. Positivity was associated with widespread fMRI deactivations at several cortical sites (including central and temporo-hippocampal areas) as well as some activation, primarily in frontal and parietal structures, and in the insula and putamen. Cortical positivity could be predicted with high accuracy by pallidum and putamen activation and supplementary motor area (SMA) and motor cortex deactivation. These findings may contribute to a better understanding of the mechanisms of SCP training in ADHD or epilepsy.

NF in ADHD

ADHD is characterised by developmentally inappropriate levels of inattention, impulsiveness and hyperactivity. It is one of the most common psychiatric disorders in children and adolescents (3–5%; Barkley, 1990; Rothenberger, Döpfner, Sergeant, & Steinhausen, 2004). Treatment usually comprises medication (e.g., methylphenidate, MPH) and/or behaviour therapy.

Numerous EEG and ERP studies have been conducted in children with ADHD. In the resting EEG, increased slow wave activity (theta) and/or reduced alpha and beta activity, especially in central and frontal regions, are most reliably associated with ADHD, most probably reflecting under-arousal of the central nervous system (for review see Barry, Clarke, & Johnstone, 2003). It seems plausible that a frequency training aiming at decreasing theta activity and enhancing beta (or SMR) activity, i.e., activating and maintaining a state of cortical arousal ('tonic activation'), might be helpful in ADHD.

ERP studies have revealed deviant processing already for early stages (latency range between 100 and 250 ms), but mainly focused on late components (for a review see Barry, Johnstone, & Clarke, 2003; Banaschewski & Brandeis, in press). The reduced P300 amplitudes observed in different paradigms could reflect attentional as well as response control deficits.

Deviations in SCPs were also reported: a decreased contingent negative variation (CNV; Grünewald-Zuberbier & Grünewald, 1982; Sartory, Heine, Müller, & Elvermann-Hallner, 2002; Banaschewski et al., 2003) and a less focused distribution of the Bereitschaftspotential (Rothenberger, Kemmerling, Schenk, Zerbin, & Voss, 1986). These findings may be in line with the dysfunctional regulation/allocation of energetical resources model of ADHD (Sergeant, Oosterlaan, & van der Meere, 1999). Children with attentional problems who performed two SCP training sessions could learn to regulate their SCPs when continuous feedback was given, but had difficulties in modulating their SCPs systematically in transfer trials; i.e., when feedback was absent (Rockstroh et al., 1990). Thus, the reduced self-regulation abilities in ADHD which may be improved by an extended SCP training were confirmed.

While the first frequency training study in children with ADHD was published as early as 1976 (Lubar & Shouse, 1976), it took more than 25 years until the effects of an extended SCP training were also investigated (Heinrich, Gevensleben, Freisleder, Moll, & Rothenberger, 2004; Leins et al., 2006). In this section, the most relevant frequency and SCP training studies conducted thus far will be reviewed. The study characteristics and main findings are summarised in Table 2. In all of these clinical studies, an improvement of ADHD symptomatology (i.e., reduction of inattention, impulsivity and hyperactivity), as well as positive effects at the cognitive level (e.g., attention), were reported. Some results indicate that NF training may have an additional effect over and above methylphenidate (MPH) medication. Thus, NF could become a useful module in multimodal treatment of ADHD.

Fuchs, Birbaumer, Lutzenberger, Gruzelier, and Kaiser (2003) and Monastra, Monastra, and George (2002) compared the effects of frequency training and MPH medication. In both studies, NF effects were at least comparable to those of MPH medication. However, in these studies parents could choose the treatment according to their preferences. A non-randomised group assignment may bias results since the choice of treatment is likely to depend on parental engagement and expectations, which may affect therapeutic success. Sample size in the study of Fuchs et al. (2003) was too small for a statistically reliable comparison between NF (frequency) training and MPH medication.

In the study of Monastra et al. (2002), the effects of NF training are impressive but can only be evaluated in association with the multimodal treatment (MPH, parental counselling and academic support) because NF was not administered without medication and behavioural treatment. It should be noted that the control group (multimodal treatment without NF) could not reach scores within the unimpaired range at the behavioural level after one year of multimodal treatment even when tested under MPH medication.

Table 2 Selected neurofeedback studies in children with ADHD. Other studies with similar designs (e.g., Rossiter & La Vaque, 1995; Kropotov et al., 2005) were not listed because they have more methodical limitations and do not make any further significant contribution

Lubar, Swartwood, Swartwood & O'Donnell (1995)	
Objective/design	behavioural, cognitive and EEG effects of frequency training; no control group; differentiation according to training success
Subjects	23 children and adolescents with ADHD (DSM-III-R); age: 8–19 years increased frontal and central theta activity and/or decreased posterior beta (13–21 Hz) activity in the resting EEG
Frequency training	40 sessions of about 60 min in 2–3 months A session was divided in a 2 min baseline period; two 5-min feedback trials, a 5-min reading trial plus feedback and a 5-min listening trial plus feedback. increase of beta (16–20 Hz) activity and decrease of theta activity; feedback electrode: FCz + CPz
Results	reduction of inattention, hyperactivity and impulsivity ($p < 0.001$); rated by parents (ADDES, McCarney 1989). Children who did not succeed to decrease theta activity were also rated as improved. improvements in continuous performance test (TOVA) and IQ test
Monastra, Monastra & George (2002)	
Objective/design	behavioural, cognitive and EEG effects of frequency training in a multimodal treatment program; no randomisation; post-treatment testing with and w/o medication
Subjects	100 children and adolescents with ADHD (DSM-IV); age: 6–19 years control group: 49 children receiving multimodal treatment w/o NF NF group: 51 children receiving multimodal treatment including NF
Treatment	one-year multimodal treatment program: methylphenidate, parent counselling, academic support, NF (optional) NF training: 34–50 sessions of 30–40 min; paradigm: see Lubar, Swartwood, Swartwood & O'Donnell (1995)
Results	MPH: average daily dose 25 mg (range: 15–45 mg/day), t.i.d. (10 - 10 - 5) larger improvement of inattention and hyperactivity for NF group, rated by parents (ADDES, McCarney 1995); virtually no improvement in the control group TOVA: comparable improvements in control group (under medication) and NF group (irrespective of status of medication) spontaneous EEG: reduction of cortical slowing (= decrease of theta/beta ratio) recorded during different conditions (e.g., resting, reading) in the NF group
Fuchs, Birbaumer, Lutzenberger, Gruzelier & Kaiser (2003)	
Objective/design	comparison of frequency training and MPH; behavioural and cognitive effects; no randomisation
Subjects	34 children with ADHD (DSM-IV); age: 8–12 years; previously untreated frequency training: 22 children; MPH: 12 children
Treatment	NF training: 36 training sessions of 30–60 minutes duration in 12 weeks paradigm depending on DSM-IV subtype: inattentive: theta decrease/beta (15–18 Hz) increase at electrode C3 hyperactive-impulsive: theta decrease/SMR (12–15 Hz) increase at electrode C4 combined type: both paradigms
Results	MPH: average daily dose 30 mg (range: 10–60 mg/day), t.i.d. (10 - 10 - 10) IOWA-Connors Behaviour Rating Scale (parents, teacher; Atkins & Milich, 1987): in both groups improvements of about 25% comparable improvements for NF and MPH in attention tests (inter alia TOVA) and intelligence test (WISC-R, German version)
Heinrich, Gevensleben, Freisleder, Moll & Rothenberger (2004)	
Objective/design	behavioural and neurophysiological effects of SCP training; waiting list control group
Subjects	22 children with ADHD (DSM-IV); age: 7–13 years; about half the children on medication SCP training group: 13 children; waiting list group: 9 children
SCP training	25 sessions of 50 minutes duration in 3 weeks 100–120 trials of 8 sec duration (2 sec baseline, 6 sec feedback) per session; negativity and positivity trials in random order; feedback electrode: Cz transfer: 40–60 transfer trials per session; dry exercises at home
Results	significant effects for the SCP training group only: ADHD rating scale – total score: 25% decrease after training; 35% decrease at 3 months follow-up cued continuous performance test (CPT-OX): decrease of impulsivity errors; increase of the contingent negative variation in cue trials
Leins, Hinterberger, Kaller, Schober, Weber & Strehl (in press)	
Objective/design	comparison of frequency training and SCP training; behavioural and cognitive effects; single-blind setting
Subjects	38 children with ADHD (DSM-IV); age: 8–13 years; 2 children on medication frequency training: 19 children; SCP training: 19 children

Table 2 Continued

NF training	<p>30 sessions divided in three blocks of two weeks</p> <p>In both training paradigms, a session consisted of about 150 trials of 8 sec length per session. As training proceeded, more activation than deactivation trials were conducted; feedback electrode: Cz</p> <p>frequency training: modulation of theta and beta (14–21 Hz) activity in both directions</p> <p>SCP training: production of negative and positive SCPs.</p> <p>Transfer: 23% transfer trials; practice of strategies at home. In the third training block, e.g. homework from school was integrated in the training.</p>
Results	<p>similar behavioural and cognitive effects for both NF paradigms after training and at 6 months follow-up:</p> <p>reduction of hyperactivity and inattention (parents), reduction of hyperactivity and impulsivity; improvement of social behavior (teacher)</p> <p>improvements in attention test (TAP, Zimmermann & Fimm, 2002) and Full Schale IQ and Performance IQ (WISC-R, German version)</p> <p>EEG control:</p> <p>SCP group: significant improvement of self regulation of negative SCPs in feedback and transfer trials; significant discrimination between positivity and negativity tasks in feedback and transfer trials</p> <p>Theta/beta group: significant improvement of reducing theta/beta ration only in feedback trials; significant improvement of discrimination between tasks in feedback and transfer trials</p>

This result is difficult to understand since this stimulant medication as state-of-the-art intervention should have contributed to the improvement. Hence, whether or not the pharmacological treatment was applied adequately must be challenged.

The IQ effects described in several studies have to be interpreted with caution. For a 3-month test–retest interval (Fuchs et al., 2003), the larger IQs are probably attributable to practice effects. In Lubar, Swartwood, Swartwood, and O'Donnell (1995), IQ scores were only assessed in a small subgroup two years after the NF training, with no information about the time between the end of NF training and IQ retesting.

The studies conducted so far do not address separation of unspecific effects (e.g., providing time and attention to the children while conducting the NF training, raising expectations of improvement; NF training is an attention-demanding task). In the study of Lubar et al. (1995), about 30% of the children and adolescents were not successful in reducing their theta activity during the course of the training. For these subjects, smaller effects were measured in the TOVA test after training but comparable improvements were rated by their parents. These findings indicate that unspecific effects may contribute to the outcome of NF and underline the importance of disentangling specific and unspecific training effects. An adequate control group or a positive correlation between regulation skills (or changes in the EEG parameters trained) and reduction of symptoms would provide evidence for specific training effects. But this issue has not yet been addressed adequately.

In the SCP training study of Heinrich et al. (2004) event-related potentials were recorded during a cued continuous performance test (CPT-OX) before and after the training.

SCP training led to a pronounced CNV increase in the cue trials of the CPT-OX test (see Figure 2),

which was not found for a waiting-list control group. Other ERP parameters (e.g., N2 or P300) were not affected by SCP training. The CNV is thought to be related to the negativities that must be generated in the NF training. So, it was concluded that children with ADHD may be able to allocate more attentional resources expecting the succeeding relevant stimulus after SCP training. The CNV increase was accompanied by a decrease of impulsivity errors. Hence, the CNV increase could reflect a neurophysiological correlate of improved self-regulatory capabilities. To date, however, it is not known to what extent a specific neurophysiological effect like the CNV

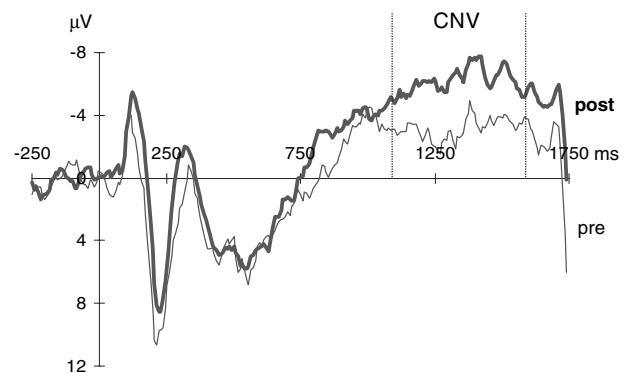


Figure 2 Grand mean event-related potentials of children with ADHD ($N = 13$) before starting a SCP training (pre; thin line) and at the end of the training course (post; thick line) in the cue condition of a continuous performance test (CPT-OX). A pronounced increase of the contingent negative variation (CNV) in the marked interval [1100 ms; 1600 ms] can be observed, probably reflecting the neurophysiological mechanism of a clinically successful training (reprinted from Heinrich, Gevensleben, Freisleder, Moll, & Rothenberger, 2004 with permission from the Society of Biological Psychiatry)

increase is actually related to behavioural effects and how long it persists.

In some studies (e.g., Fuchs et al., 2003) specific NF paradigms were applied for ADHD subtypes. This seems to be a reasonable approach although not yet validated by empirical data. Determining which paradigm could be the most effective for a clinical (or possibly neurophysiological) ADHD subtype will have to be studied systematically.

The question may arise whether theta/beta or SCP training is more efficacious in ADHD. Leins et al. (2006) compared theta/beta training and SCP training. The groups differed with regard to the acquired skill to control the EEG parameter used for NF training but showed comparable behavioural and cognitive improvements which were also measurable at a 6-month follow-up. Children of both groups were told to find strategies to 'activate' and to 'deactivate' their brain. Thus, theta/beta training also comprised modulation in both directions, i.e., decrease of theta activity and increase of beta activity in the activation condition and vice versa in the deactivation condition. This is in contrast to other studies in which tonic activation is trained in trials lasting for several minutes.

At the neurophysiological level, a differential pattern may be expected for theta/beta training and for SCP training, namely a P300 increase after theta/beta training (with long trials) according to the results of Egner and Gruzelier (2004) in healthy adults and a CNV increase after SCP training (Heinrich et al., 2004). This differential neurophysiological pattern corresponds to the concept that theta/beta training aims at tonic aspects of arousal whereas SCP training is related to phasic regulation of excitability underlying attentive behaviour. As described in the example of the musician in the introduction section, both aspects are important for optimal performance. Thus, it could also be interesting to run a combination of theta/beta and SCP training in ADHD.

In summary, the evidence base for the clinical efficacy and effectiveness of theta/beta training and SCP training has clearly improved in recent years. Further studies are necessary to control for unspecific effects and confounding variables (e.g., parental engagement), also taking the long-term outcome into account.

NF in epilepsy

Epilepsy is a central nervous system disorder characterised by unprovoked, recurrent seizures that may affect physical, mental, or behavioural functioning. This diverse disorder often starts in the first decade of life (prevalence in children: .5%). Most epileptic syndromes are grouped into two basic categories: partial and generalised. Partial (focal) seizures occur within a localised area of the brain, whereas generalised seizures appear throughout the

forebrain from the outset. Negative SCP shifts indicating increased cortical excitability facilitate paroxysmal activity over cortical tissue.

Antiepileptic drugs are primarily used in the treatment of epilepsies. However, at least 20 to 30% of all patients with epilepsy continue to experience seizures after medication management and are considered drug-resistant. Individuals with intractable epilepsy often suffer from focal seizures and only 3% of these patients are candidates for surgical intervention. About two-thirds of all neurosurgical interventions for epilepsy result in complete remission of seizures. Hence, at least 15% of all patients with epilepsies are not adequately treated by standard interventions (Mattson, 1992; Sander & Sillanpää, 1998; Stodieck & Wieser, 1987).

Frequency training. A potential antiepileptic effect of SMR training was initially discovered by chance from animal studies (Serman, 1976). Using operant conditioning, cats were trained to increase their 12–15 Hz sensorimotor activity, which typically occurs over the somatosensory cortex in alert but motionless cats. As these animals were included in another study dealing with convulsive properties of toxic hydrazine compounds, they were found to be resistant to hydrazine-induced seizures despite showing the usual toxic prodrome. These observations served as motivation to test an antiepileptic effect of SMR training in patients.

Several SMR training studies have been published (for review see Walker & Kozlowski, 2005), e.g., a double crossover, single-blind (ABA) design study by Serman and MacDonald (1978). Different frequency bands (6–9 Hz and either SMR (12–15 Hz) or 1–23 Hz) were considered. Activity had to be increased in one band and decreased in the other in a sample of 8 patients (aged 18–35) with poorly controlled seizures (bipolar feedback channel C3–T3; left central/temporal electrodes). The study consisted of successive 3-month training periods, with training paradigms reversed after each period without the subject's knowledge. Seventy-five per cent of the patients reported significant and sustained seizure reductions, following an increase for either SMR or 18–23 Hz activity while reducing 6–9 Hz activity.

Responses were specific for the SMR paradigm only, with seizure rates returning to baseline when the training paradigm was reversed. The authors concluded that a non-specific interpretation of these effects should be rejected in favour of an EEG normalising hypothesis.

For a modified SMR training (increase of 12–18 Hz and decrease of 4–8 Hz), Tozzo et al. (1988) reported a significant decrease in seizure frequency in 5 of 6 patients compared to multiple baseline phases without treatment. In four of the patients a significant negative correlation between SMR increase and decrease of seizure rates could be demonstrated, indicating specific SMR training effects.

However, these studies are not sufficient to establish the clinical efficacy of SMR training in epilepsy. Only a few of the studies are controlled, the sample size is often small, details about sample characteristics are partly missing and follow-up data are deficient.

SCP training. Based on the model of increased cortical excitability in epilepsy, an SCP training aimed at using positivity shifts (which means suppression of negativity), in order to prevent seizures, has proven to be an effective adjunctive treatment option for epilepsy in a series of publications by Birbaumer and co-workers (e.g., Elbert, Birbaumer, & Rockstroh, 1990; Kotchoubey et al., 1996; Kotchoubey et al., 2001; Rockstroh et al., 1993; Strehl, Kotchoubey, Trevorrow, & Birbaumer, 2005). In these studies, patients (mainly adults) with drug-resistant epilepsies were included. It was reported that patients with epilepsy learn SCP regulation more slowly than healthy subjects and that SCP training leads to a decrease of seizure frequency, with some patients even becoming seizure-free. To control for non-specific effects, SCP training was compared to alpha band training (Birbaumer et al., 1992). Seizure frequency decreased only after SCP training.

In this review, we focus on the latest of these studies that has the most sophisticated design. The results of this study were presented, e.g., in Kotchoubey et al. (2001) and in Strehl et al. (2005). SCP training was compared with respiration feedback (RES) and medication (MED). Both feedback programs were integrated in a behavioural self-management program. So-called placebo scales (e.g., satisfaction with therapy) were assessed to control for non-specific training effects. Finally, the study also analysed the stability of cortical self-regulation (Kotchoubey, Blankenhorn, Froscher, Strehl, & Birbaumer, 1997) and predictors of clinical outcome (Strehl et al., 2005).

For ethical reasons, group assignment was not random. This strategy led to uneven distributions among treatment groups (SCP training: $N = 34$; medication: $N = 7$; respiration feedback: $N = 11$) and also to some group differences before treatment without substantially affecting results.

SCP training comprised 35 sessions with a larger portion of positivity trials in the second half of the training. It was integrated in a behaviour training which was intended to increase patients' awareness of antecedents of seizure behaviour, to change reinforcing contingencies and to apply the learned SCP self-regulation skills in real-life situations.

After one year (follow-up), there was a significant reduction in the number of seizures per week (mainly determined by simple partial seizures) in the SCP training group (pre: 3.30 ± 1.01 ; follow-up: $2.19 \pm .48$) and the medication group (pre: $1.83 \pm .39$; follow-up: $.84 \pm .21$), but not in the respiration feedback group (pre: 6.87 ± 3.59 ; follow-up: $7.92 \pm$

1.86). During treatment, patients evaluated parameters like their satisfaction with the therapy or their intention to recommend the treatment to other patients repeatedly. These placebo scales increased in all three groups to a comparable amount during the course of treatment and, thus, could not account for clinical improvement (i.e., seizure reduction) as a main factor.

Data from the SCP group were further analysed. Each patient's seizure frequency was evaluated by means of a sequential analysis in a week-by-week sequence for a follow-up period of one year. Patients were divided into an 'improvement class' (= statistically significant seizure reduction of at least 50%; $N = 14$), an 'indefinite class' (= non-significant seizure reduction; $N = 8$), and a 'failure class' (= consistently failed to reach 50% improvement; $N = 12$); i.e., about 65% of the patients benefited from SCP training.

Seventy per cent of treatment success could be predicted by three variables:

1. cortical excitability (negativity) at the beginning of training (poor prognosis);
2. epileptic focus (left temporal focus → poor prognosis; however, the two patients who became seizure-free also had a left temporal focus);
3. personality variables (lower satisfaction with life and negative emotionality → better prognosis).

Reduction of complex partial and secondary generalised seizures covaried with SCP control attained in the last training session. Patients with these seizure types were more likely to experience seizure reduction if they demonstrated good SCP control at the end of training (Strehl et al., 2005).

The positive outcome of SCP training for drug-resistant patients with bilateral and multiple epileptic foci in the study of Kotchoubey et al. (2001) deserves particular attention. This finding supports the assumption that a physiological change (reduced excitability within the cortico-striato-pallido-thalamo-cortical loop; see also Hinterberger et al., 2003 and Strehl et al., 2006, for epilepsy patients who are able to self regulate SCPs) mediates the therapeutic effect in these patients.

For patients difficult to treat with antiepileptic drugs or by neurosurgery, SCP training integrated in a behavioural self-management program offers an evidence-based alternative. However, SCP training is not yet a well-established method in the treatment of epilepsy. So far, studies mainly included adult epilepsy patients. In future studies, whether NF (SCP) training can lead to comparable effects in children will have to be tested.

NF in other child psychiatric disorders

In tic disorders, NF is also practised but the only publication concerning it is a case report. Two patients (14 and 32 years old) became free of tics after

SMR training (Tansey, 1986). Though these results seem to be promising, it must be taken into account that tic psychopathology is time-varying: Tics wax and wane and during adolescence a steady decline in tic frequency and severity can often be observed (Leckman, Vaccarino, Kalanithi, & Rothenberger, 2006; Rothenberger & Banaschewski, 2006). Therefore, it is essential to conduct controlled treatment studies. Recently, a study funded by the Tourette Syndrome Association has started to compare the effects of SMR and electromyographic (EMG) training (40 sessions) using a double-blind design (Strohmayr, 2004).

Patients with anxiety were trained either to increase alpha activity or to decrease alpha activity (Plotkin & Rice, 1981; Rice, Blanchard, & Purcell, 1993). For both paradigms, patients reported a significant reduction in anxiety. Thus, the results argue against the specificity of the effects of alpha training in anxiety.

Raymond, Varney, Parkinson, and Gruzelier (2005) reported that a theta/alpha training (compared to yoked control training) improved mood in socially anxious students, indicating a potential benefit of this paradigm in anxiety. In EEG studies, anxious girls showed larger right than left frontal activation in the lower alpha band (8–10 Hz), whereas in healthy girls no asymmetry or opposite asymmetry was observed (Baving, Laucht, & Schmidt, 2002). So, there might also be an indication to use age- and gender-specific paradigms taking frontal asymmetry in the alpha band into account.

NF might also be useful in autism (Scolnick, 2005), schizophrenia (Gruzelier, Hardman, Wild, & Zaman, 1999) and learning disabilities (Fernandez et al., 2003) where first investigations have been published. For other disorders (post-traumatic stress disorder, attachment disorder, conduct disorder, eating disorder, fetal alcohol syndrome), more or less anecdotal reports are available. In principle, a pathophysiological model should underlie the application of NF for a certain disorder.

General comments and future perspectives

Neurofeedback which directly targets the interface of brain-behaviour interaction may become an additional treatment option for children and adolescents with neuropsychiatric disorders characterised by self-regulation deficits. In addition, 'normal' subjects may improve cognitive functions (e.g., attention and working memory) and performance in real-life situations by means of NF.

Design of evaluation studies

In further studies, randomised, controlled trials have to be conducted to, inter alia, disentangle specific and unspecific effects of NF at the clinical (beha-

vioural) level. From a methodical point of view, a yoked-control design (placebo training) would be best. In such training, a subject seems to receive feedback calculated from his own brain electrical activity. But, in reality, it is either a random pattern or the recording of another subject is used. However, such a placebo condition raises ethical questions and does not seem feasible, particularly in the treatment of children. Depending on the disorder under study, alternative designs seem to be appropriate. In ADHD, for example, a computer-based attention training or feedback of peripheral parameters (e.g., electrodermal activity) may be used as a control condition. In tic disorders, a comparison of NF training with EMG biofeedback training could be appropriate.

Additionally, NF could be compared with established interventions (medication, behaviour therapy) using sufficient sample sizes. A crossover design may be chosen but it does not allow adequate investigation of long-term effects.

It is recommended to assess expectation and satisfaction with therapy in all treatment conditions. These kinds of 'placebo scale' was used, for example, in the epilepsy study of Kotchoubey et al. (2001) in which it was shown that they did not contribute to clinical outcome. Finally, long-term effects (clinical outcome, spectral EEG analysis, neuromodulatory skills) should be investigated using at least a 6-month follow-up interval.

Training paradigms and new developments

Training paradigms have to be optimised, i.e., the best possible paradigm for an individual patient or a certain clinical or neurophysiological (e.g., spectral EEG profile) subtype of a disorder has to be investigated systematically. In this context, it is necessary to study to what extent frequency and SCP training paradigms address the same or differential processes or whether they could complement each other.

Since in several child psychiatric disorders decreased left/right asymmetries can be found (e.g., neurophysiologically in ADHD and tic-disorders; Rothenberger & Kemmerling, 1986), NF-paradigms adapted to this issue might help to improve lateralisation and thus behaviour (see Elbert et al., 1984 for healthy adults).

Using multi-channel NF systems, it will be interesting to consider training paradigms taking spatial information (e.g., LORETA (low-resolution electromagnetic tomography) neurofeedback; Congedo, Lubar, & Joffe, 2004) or interactions between different brain regions (e.g., NF with EEG measures like coherence (Nunez et al., 1997) or neural synchrony (Le Van Quyen et al., 2001)) into account. Thus, a battery of paradigms may be developed allowing miscellaneous cognitive and neuronal (dys)functions to be trained specifically.

Some efforts have been started to implement fMRI (functional magnetic resonance imaging) neurofeed-

back. It has already been demonstrated that it is technically feasible, i.e., that online feedback can be calculated reliably (Weiskopf et al., 2003) and that it is possible to learn voluntary control over activation in a specific brain region (the rostral anterior cingulate cortex) probably leading to control over pain perception (deCharms et al., 2005). Of course, fMRI neurofeedback is too expensive to become attractive for clinical practice. A cheaper alternative could be the so-called HEG (hemoencephalography) neurofeedback which is based on the principle of near-infrared spectroscopy allowing regional cortical but not subcortical activation to be fed back (Obrig et al., 2000; Tinius, 2005). Thus, NF based on functional imaging could offer new treatment options in addition to EEG-based paradigms which basically have better temporal resolution (Banaschewski & Brandeis, in press).

Transfer into everyday life

The results of the NF studies in healthy participants, children with ADHD and patients with epilepsy reviewed in this article clearly argue for the generalisability of NF effects to performances and behaviour in real-life conditions.

In SCP training, where phasic self-regulation skills are acquired, practice in transferring these skills into everyday life, i.e., when and how to apply the learned strategies and link their use to cues, respectively, seems to be important. With time, this process may work automatically. In frequency training where tonic aspects are addressed it might be speculated that neuromodulation per se accounts for the therapeutic success in the sense of improving a neuronal dysfunction. On the other hand, it is not known whether neuroregulation is learned in a state-dependent manner and, thus, performance is restricted to the training setting if transfer into daily life is not implemented.

NF training is aiming at basic mechanisms. Applying the strategies learned in the training should directly induce a better functional state. Thus, generalisation might be accomplished more easily than for other behaviour trainings.

NF and multimodal treatment

In the major part of patients, NF training as the only intervention might not be sufficient to achieve optimal clinical (behavioural) improvement. So, it should rather be implemented in a multimodal treatment programme, further including, e.g., parental counselling, cognitive behavioural therapy, and/or medication according to individual requirement. For the treatment of epilepsy, SCP training has already been integrated successfully in a behavioural self-management program (Kotchoubey et al., 2001). Comparable combined approaches should also be developed for other disorders. On the other hand, in

some patients, clinical (behavioural) improvement after NF training is large enough so that no further intervention is necessary. It is conceivable that patients will do NF training partly at home ('home treatment'). On all accounts NF training, as any other psychotherapeutic method, should be introduced and, later on, supervised by a clinician.

Central nervous mechanisms of NF

Research should not only concentrate on questions concerning the clinical efficacy of NF but also address the topic of the central nervous mechanisms underlying successful training. The CNV increase in children with ADHD after SCP training (Heinrich et al., 2004) as well as the P300 increase in healthy adults after beta (15–18 Hz) training (Egner & Gruzelier, 2004) may reflect specific neurophysiological effects of these two training paradigms. These findings lead to two conclusions. First, it is possible to measure training effects at the brain level and, second, ERPs recorded in cognitive tasks are an appropriate tool for it. Applying functional imaging approaches may reveal additional knowledge about the neural networks modulated by a successful NF training. Levesque, Beauregard, and Mensour (2006) provide preliminary data for this approach. They report changes in the anterior cingulate cortex of children with ADHD who participated in theta/beta and theta/SMR training.

Summary

Many questions concerning clinical efficacy and the mechanisms underlying successful NF training in neuropsychiatric disorders remain to be solved; however, this does not argue against NF. The same holds true for psychopharmacological interventions despite the fact that large resources have been spent for quite a long time to address these issues. These questions should rather serve as motivation for further, more intensive activities in this exciting field of treatment and basic clinical research.

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